REMARKS

On November 20, 2006, the Examiner mailed a Final Office Action. Applicants responded by filing a request for reconsideration. No Advisory Action had been received by Applicants' Representative as of May 18, 2007. In a telephone conversation with the Examiner on May 18, 2007, Applicants' Representative was advised that the arguments made in the paper of March 30, 2007 were not persuasive.

Status Of The Claims

Claims 1-25 are pending in the application. A minor editorial amendment is made to claim 5. New claim 25 is supported by the specification at, e.g. the first paragraph on page 12 of the English translation of the specification, and by Figure 2, panels a-f.

Rejection Under 35 U.S.C. §103(a)

Claims 1-24 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Griffin et al. (EP 0 010 987) (hereinafter Griffin '987) in view of Biegajski et al. (U.S. 5,700,478) (hereinafter Biegajski '478). This rejection is respectfully traversed. Applicants have previously argued as follows:

> The Examiner asserts that Griffin '987 discloses a rolled up preparation for the controlled release of an active agent in the body. The Examiner further asserts that the drug-containing layer is attached to a carrier, rolled and delivered to the patient. The Examiner contends that the particular release profiles "can be determined through routine experimentation". The Examiner acknowledges that Griffin '987 does not disclose the addition of a pressure-sensitive adhesive layer and relies on the teachings of Biegajski '478 to overcome this deficiency, asserting that the inclusion of a pressure-sensitive adhesive layer would be obvious to one skilled in the art "since they would want the unfolded patch to adhere to the delivering surface".
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> Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the teachings of the references to obtain the invention. Second, there must be a

reasonable expectation of success in making the invention. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants initially note that, contrary to the Examiner's assertion, Griffin '987 does not disclose a rolled up preparation for the **controlled** release of an active agent in the body. Griffin '987 is directed to a device for the **sustained** release of a veterinary medicament (see Griffin '987 at page 1, lines 1-2, page 3, lines 8-11, page 4, lines 25-27 and page 8, lines 37-38). The term "sustained release" refers to cases where the release of a drug is extended in time, but without achieving a particular release profile (i.e. time course of release of drug). In contrast, devices for controlled drug delivery are designed so as to adjust the rate and duration of drug delivery, thus providing the required drug delivery profile. As disclosed by Griffin '987, the sustained-release device is designed in a first shape in which it is restrained in a rolled or folded form, or a second shape in which it is unrolled or unfolded. The device is designed such that conversion of the first shape into the second shape will occur immediately once the device has arrived at its destination (the rumen of an animal). This shape conversion must occur immediately to ensure that the device will be retained within the rumen (see Griffin '987 at page 3, lines 17-18). Release of the active substance takes place only when the device has assumed its second shape, i.e. when it is fully unfolded or unrolled. Accordingly, the active substance is released through the entire area of the sheet in which it is uniformly distributed and the release is sustained due to the erosion properties of the sheet material. One skilled in the art would realize that, because the release of the active substance occurs through the entire area of the sheet, the device of Griffin '987 can **only** provide sustained release **but not controlled release.**

Furthermore, Applicants respectfully submit that one skilled in the art would not be motivated to modify the device of Griffin '987 to provide a controlled release of an active agent, absent impermissible hindsight gleaned from Applicants' disclosure. Although the Examiner asserts that "the particular release profiles can be determined through routine experimentation and changed to fit the needs of the patient", the passage from Griffin '987 referred to by the Examiner (page 5, 1-14) merely describes how the erosion characteristics of the erodable sheet can be varied by incorporating a biodegradable material. By doing so, the duration of the "sustained release" can be adjusted. However, Griffin '987 fails to teach or suggest any "release profiles" or **controlled** release. Therefore, contrary to the Examiner's assertion, such "particular release profiles" cannot be determined through routine experimentation. Modifying the teachings of Griffin '987 by "routine experimentation" as suggested by the

Examiner, would only result in devices having a different duration of sustained release, but not in devices for controlled release of an active agent.

The Examiner acknowledges that Griffin '987 does not teach or suggest the inclusion of an adhesive layer, as presently claimed. As previously discussed, Griffin '987 teaches away from the inclusion of an adhesive layer, as it teaches that stickiness is a problem which should be avoided. The Examiner argues that "the inclusion of a pressure-sensitive adhesive however would have been obvious... since they would want the unfolded patch to adhere to the delivering surface". However, Applicants respectfully submit that this argument is inappropriate, since the devices disclosed by Griffin '987 are specifically adapted to be administered to ruminant animals and to be retained in the rumen of these animals. Retention is achieved by increase in size (i.e. when the device unrolls to assume its "second shape"). The inner wall of the rumen is generally very uneven, having ridges and finger-like protrusions, and the wall is almost constantly moving to ensure that the food becomes thoroughly mixed. In addition, when the animal ruminates, the rumen contracts to expel a portion of the partly digested food to the esophagus and mouth. Hence, a person of ordinary skill in the art would never consider the idea of trying to adhere a patch to the inner surface of the rumen.

Biegajski '478 fails to cure the deficiencies of Griffin '487. The term "pressure-sensitive adhesive" relates to adhesives which develop bonding power upon application of pressure. As disclosed by Biegajski '478, it is necessary to apply pressure in the area of the body where the device needs to be adhered to. Clearly, it is not possible to apply such pressure from inside the rumen, stomach or intestine of a human or animal. As was noted by the Examiner (see outstanding Office Action at page 3, section 3), the devices of Biegajski '478 are useful for delivery of substances to the mouth, rectum or vagina, which are body orifices that can be easily accessed from outside by using fingers for applying pressure to affix the pressure-sensitive device to the mucosal surface. This would clearly not be possible when administering the device to the rumen, or to the inner wall or any other internal organ of the body.

Furthermore, the Examiner has failed to explain why the skilled person would want the unfolded patch to adhere to the "delivering surface". Obviously, adherence is not required for retention, since the device is already retained by its extended area size after unwinding. Therefore, since the primary reference teaches against incorporating adhesive substances, and since it is neither desirable nor practically possible to adhere a device to the inner wall of the rumen (or any other organ of the gastrointestinal system) by pressure-sensitive adhesion, it would not have been obvious to add a pressure-sensitive adhesive layer to the device of Griffin '987. The Examiner's argument appears to be based on hindsight knowledge derived from the present application. The Examiner states that "the Griffin reference does not teach against adhesiveness,

but merely away from incomplete unfolding". However, it is quite clear that if the device, after having arrived in the rumen, unfolds only partially and slowly ("whenever that occurs"), it will not be retained in the rumen but will be expelled when the animal ruminates, or will move on to the next part of the digestive tract. Therefore, adhesiveness must be avoided to ensure proper function of the device disclosed by Griffin '987.

In addition, Applicants submit that outstanding claim 1 requires that the width of the active substance-containing layer, and/or the concentration of active substance in this layer is not constant in relation to the longitudinal extension of the layer. The Examiner has suggested that the films of Biegajski '478 would have a non-uniform contour for providing an improved fit, and that incorporation of a thus-shaped adhesive layer into the rolled device of Griffin '987 would result in a device having a non-uniform width, as presently claimed. However, this is highly speculative since, the shape of the "application situs" is not well defined by Griffin '987. The lumen of the rumen is constantly changing due to the movements of the muscle layer surrounding the rumen (which movements are required for mixing the food to be digested). Assuming, *arguendo* that the device of Griffin '987 is provided with a pressure-sensitive adhesive layer, it would be practically impossible to arrange the device within the rumen such that its contour would fit the contour of the rumen. Hence, the skilled person would never consider the idea of providing the device of Griffin '987 with a particular shape to fit the application situs (the rumen). In addition, Applicants submit that the cited documents do not suggest that the width of the active substance-containing layer is variable with respect to the longitudinal dimension which, according to the present invention, is essential for obtaining the desired release profile during progressive unfolding or unrolling of the device.

The Examiner further asserts that "the features upon which Applicants relies (i.e., timed delivery, slow unfolding, a specific release profile) are not recited in the rejected claim(s)". However, Applicants note that these functional features are due to the presence of a liquid-soluble adhesive layer, as presently claimed in claim 1, which controls the unwinding of the device. The unwinding speed, together with the non-constant width or active substance concentration (claim 1, section (b)), results in a time-dependent release profile. Since the two cited documents, even when applied in combination, do not suggest at all the incorporation of an adhesive layer for controlling the unrolling speed device, these documents could not imply the functional features of timed delivery or specific release profile.

Clearly, the cited references, alone or in combination, fail to teach or suggest every limitation of the claimed invention. For this reason alone, this rejection is improper and should be withdrawn. Furthermore, one of ordinary skilled in the art would not be motivated to combine the references or to modify them by adding an adhesive layer and further by giving a non-uniform shape to

the device. Courts have clearly established that, even when a combination of references teaches every element of a claimed invention, a rejection based on a *prima facie* case of obviousness is improper absent a motivation to combine. *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998). The release profiles obtained by the device of the present invention are due to the combined presence of a liquid-soluble adhesive layer and an active substance-containing layer having a non-uniform width or concentration in the longitudinal direction. This combination of features is not obvious to a person of ordinary skill in the art being familiar with the teachings of Griffin '987 and Biegajski '478 but not with the teaching of the present invention. Although the Examiner contends that "the layers would be added to the Griffin invention in order to improve the adhesion and placement of the unrolled drug delivery device", neither Griffin '987 nor Biegajski '478 suggest a device which is first unrolled and then affixed to the application side by pressure. Such devices would be extremely difficult to handle under practical conditions, and, therefore, the skilled person would not have considered the proposed combination.

Because the invention, as set forth in Applicants' claims 1-24, is not disclosed or made obvious by the cited prior art, reconsideration and withdrawal of this rejection are respectfully requested.

To the above remarks, Applicants add that the Examiner should consider Figures 2a-g, which show that by varying the shape of the active substance containing layer, the temporal release profile can be changed.

Furthermore, the Examiner has previously indicated that Applicants' arguments about the temporal profiling of the release have not been persuasive because this aspect of the invention was not recited in the claims. Applicants have at this time added new claim 25, which expressly recites this feature of the invention. Applicants submit that at least new claim 25 should be found allowable over the prior art of record. As to the previously pending claims, Applicants note that at least claim 1 describes that the width and/or concentration of the active substance layer is variable along the longitudinal (unrolling) direction of the preparation. Also, claim 6 describes a variable concentration profile of the active substance and claim 20 describes

distributing the active substance in a variable manner along the longitudinal extent of the preparation. The variable distribution of active substance provides a temporal variation in release, i.e. controlled release, as Applicants have argued.

Applicants submit that, in view of the above amendments and remarks, the present claims are patentable over the prior art of record. The favorable actions of withdrawal of the standing rejection and allowance of the application are requested.

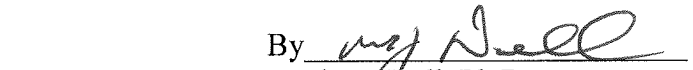
Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell (Reg. No.36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. 1.17 and 1.136(a), the Applicant has petitioned for an extension of three months to May 20, 2007 for the period in which to file a response to the Final Office Action dated November 20, 2006. Because May 20, 2007 falls on a Sunday, this response is timely submitted. The required fee has been paid in connection with the proper filing of this response.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Dated: May 21, 2007

Respectfully submitted,

By 

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